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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/889,742 | 07/20/2001 | Kazuhito Miyauchi | 2603.2 | 9051 |

5514 7590 12/22/2003

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| EXAMINER |
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SAUCIER, SANDRA E

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| ART UNIT | PAPER NUMBER |
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1651

DATE MAILED: 12/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/889,742

Applicant(s)

MIYAUCHI ET AL.

Examiner

Sandra Saucier

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1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 26-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 26-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10/2/03.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Claims 26–51 are pending and are considered on the merits.

Claim Rejections – 35 USC § 112

INDEFINITE

Claims 28 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Please note that the same agent, “polyoxyethylene glycol derivatives which is a low foaming wetting penetrant” which may be the reagent in step 1, is said to be used for inhibiting both the determination of HDL and LDL. This appears to be an error. Please see claims 28 and 41 and the specification at page 12, line 7 and last line. These agents should be specific for a particular lipoprotein. The use of the exact same agent to inhibit the reaction of both LDL and HDL, while allowing assay of either LDL or HDL appears to be an error.

Claim 41 uses “forming” instead of foaming. Also, if the plural of derivative is used, the claim should state “which are”.

Claim Rejections – 35 USC § 103

Claims 26–51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida *et al.* [U] or Ohkubo *et al.* [W] in view of US 4,215,993 [A] or EP 76211 [O].

The claims are directed to a method for quantitating triglycerides in a particular lipoprotein in a sample containing a mixture of lipoproteins comprising:

eliminating the free glycerol from a sample containing free glycerol and triglyceride in the particular lipoprotein,

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reacting the resultant sample with lipoprotein lipase, in the presence of a reagent which inhibits the reaction of lipoproteins other than the particular lipoprotein, to produce glycerol from the triglyceride,

reacting the sample with an enzyme system which generates H_2O_2 from the produced glycerol, and

quantitating the H_2O_2 .

The references are relied upon as explained below.

Yoshida *et al.* disclose a method for the determination of triglyceride concentration in a sample with free glycerol comprising:

eliminating the free glycerol from the sample using glycerol kinase, glycerol 3-phosphate oxidase to generate H_2O_2 ,

allowing the resultant sample to react with lipoprotein lipase, glycerol oxidase and peroxidase and developing color with p-chlorophenol, 4-aminoantipyrine and measuring the color intensity which is correlated with triglyceride concentration in the sample.

Ohkubo *et al.* disclose a method for the determination of triglyceride concentration in a sample with free glycerol comprising:

eliminating the free glycerol from the sample using glycerol oxidase and peroxidase to generate H_2O_2 ,

allowing the resultant sample to react with lipoprotein lipase and peroxidase and developing color with 4-aminoantipyrine and EMAE and measuring the color intensity which is correlated with triglyceride concentration in the sample.

The primary references lack the use of polyanions/detergents to select a particular lipoprotein for the determination of triglyceride concentration.

US 4,215,993 discloses a method of separating various lipoprotein fractions from serum using polyanions in order to determine the concentration of lipoprotein components by desired methods (claims 17 and 23 and col. 1, l. 15).

EP 76211 discloses a method of separating various lipoprotein fractions from serum using polyanions/divalent cations or detergents in order to determine the individual fractions' components such as triglyceride (abstract).

The use of the methods described in US 4,215,993 or EP 76211 to isolate a particular lipoprotein fraction in order to quantitate the triglyceride concentration in that particular lipoprotein fraction by the method of Yoshida *et al.* or Okuba *et al.* would have been obvious at the time of invention to one of ordinary skill in the art because EP 76211 suggests the use of polyanions and/or detergents for the determination of triglycerides in specific lipoprotein fractions (abstract).

Further, US 4,215,993 specifically states that the use of polyanions with serum to precipitate high density lipoproteins allows for determination of triglyceride by a desired method, which may be the determination disclosed by Yoshida *et al.* or Okubo *et al.*

One of ordinary skill in the art would have been motivated at the time of invention to perform the claimed method in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

All elements of the claimed method are disclosed in the prior art.

Response to Arguments

Applicant's arguments filed 10/2/03 have been fully considered but they are not persuasive.

Applicants argue that the methods of US 4,215,993 and EP 76211 disclose separating a particular lipoprotein from a mixture by centrifuging, isolating the sample and then reaction with enzymes to quantitate triglyceride. The example 1 of '993 does exemplify a mixture of lipoproteins in a serum sample which is treated with a precipitating reagent which leaves HDL in the supernatant, and it is the supernatant that is reacted with the enzymes for quantitating X in the particular lipoprotein, as applicants point out.

However, the claimed method only requires that the sample from step 1 is reacted with LPL in the presence of a reagent which inhibits reaction with LPL except for the particular lipoprotein. As the sample from step 1 is not required to contain a mixture of lipoproteins, and some aggregating agent is still present in the supernatant during the addition of quantifying enzymes as shown in the reference, the instant claim limitations are fulfilled.

Applicants argue that the references do not relate to enzymatically quantitating a particular lipoprotein in a sample containing a lipoprotein other than the particular lipoprotein. This is not persuasive since serum clearly contains a mixture of lipoproteins and it is the sample which is enzymatically quantitated.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

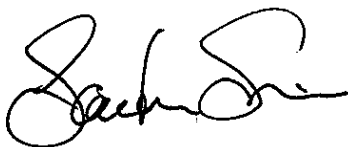
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is

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filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651. The supervisor for 1651 is M. Wityshyn, (703) 308-4743. The normal work schedule for Examiner Saucier is 8:30 AM to 5:00 PM Monday and Tuesday and 8:30 AM to noon on Wednesday.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. Status inquiries must be directed to the Customer Service Desk at (703) 308-0197 or (703)-308-0198. The number of the Fax Center for the faxing of official papers is (703) 872-9306.

A handwritten signature in black ink, appearing to read 'Sandra Saucier', with a stylized, cursive script.

Sandra Saucier

Primary Examiner

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December 17, 2003